Potential bioterrorism agent: Category B

ENCEPHALITIS, VIRAL

Arthropod-borne viral encephalitis

DISEASE REPORTING

In Washington

The last human case of arthropod-borne viral encephalitis reported in Washington was western equine encephalitis in 1988. Saint Louis encephalitis has also occurred in Washington State.

Purpose of reporting and surveillance

- To distinguish arboviral infections acquired locally from those related to travel.
- To better understand the epidemiology of these infections in Washington State and target mosquito control measures.
- To identify emerging arboviral infections in Washington, including West Nile virus.

Reporting requirements

- Health care providers: notifiable to Local Health Jurisdiction within 3 work days
- Hospitals: notifiable to Local Health Jurisdiction within 3 work days
- Laboratories: no requirements for reporting
- Local health jurisdictions: notifiable to DOH Communicable Disease Epidemiology within 7 days of case investigation completion or summary information required within 21 days. ***If bioterrorism is suspected, case must be immediately reported to DOH: 1-877-539-4344***

CASE DEFINITION FOR SURVEILLANCE

Clinical criteria for diagnosis

Arboviral infection may be asymptomatic or may result in illness of variable severity sometimes associated with central nervous system (CNS) involvement. When the CNS is affected, clinical syndromes ranging from febrile headache to aseptic meningitis to encephalitis may occur, and these are usually indistinguishable from similar syndromes caused by other viruses. Arboviral encephalitis is characterized by fever, headache, and altered mental status ranging from confusion to coma with or without additional signs of brain dysfunction (e.g. paresis or paralysis, cranial nerve palsies, sensory deficits, abnormal reflexes, generalized convulsions, and abnormal movements).

Laboratory criteria for diagnosis

- Fourfold or greater change in virus-specific serum antibody titer, or
- Isolation of virus from or demonstration of specific viral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid, or
- Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF by antibody-capture enzyme immunoassay (EIA), or
- Virus-specific IgM antibodies demonstrated in serum by antibody-capture EIA and confirmed by demonstration of virus-specific serum immunoglobulin G (IgG) antibodies in the same or a later specimen by another serologic assay (e.g., neutralization or hemagglutination inhibition).

Case definition

- Probable: an encephalitis case occurring during a period when arboviral transmission is likely, and with the following supportive serology: 1) a single or stable (less than or equal to twofold change) but elevated titer of virus-specific serum antibodies; or 2) serum IgM antibodies detected by antibody-capture EIA but with no available results of a confirmatory test for virus-specific serum IgG antibodies in the same or a later specimen.
- Confirmed: an encephalitis case that is laboratory confirmed

Because closely related arboviruses exhibit serologic cross-reactivity, positive results of serologic test using antigens from a single arbovirus can be misleading. In some circumstances (e.g., in area where two or more closely related arboviruses occur, or in imported arboviral disease cases), it may be epidemiologically important to attempt to pinpoint the infecting virus by conducting cross-neutralization tests using an appropriate battery of closely related viruses. This is essential, for example, in determining that antibodies detected against St. Louis encephalitis are not the result of an infection with West Nile (or dengue) virus, or vice versa, in areas where both of these viruses occur.

The seasonality of arboviral transmission is variable and depends on the geographic location of exposure, the specific cycles of viral transmission, and local climatic conditions. Reporting should be etiology-specific (see below; the six encephalitides printed in bold are nationally reportable to CDC):

- **St. Louis encephalitis**
- **West Nile encephalitis**
- **Powassan encephalitis**
- **Eastern equine encephalitis**
- **Western equine encephalitis**
- **California serogroup viral encephalitis** (includes infections with the following viruses: LaCrosse, Jamestown Canyon, Snowshoe Hare, Trivittatus, Keystone, and California encephalitis viruses)
- Other viral CNS infections transmitted by mosquitoes, ticks, or midges (e.g., Venezuelan equine encephalitis and Cache Valley encephalitis)

A. DESCRIPTION

Mosquito-borne viral encephalitides, Japanese encephalitis, western equine encephalitis; eastern equine encephalitis, St. Louis encephalitis, Murray Valley encephalitis, Lacrosse encephalitis, California encephalitis, Rocio encephalitis, Jamestown Canyon encephalitis, snowshoe hare encephalitis

1. Identification

A group of acute inflammatory viral diseases of short duration involving parts of the brain, spinal cord and meninges. Signs and symptoms of these diseases are similar but vary in severity and rate of progress. Most infections are asymptomatic; mild cases often occur as febrile headache or aseptic meningitis. Severe infections are usually marked by acute onset, headache, high fever, meningeal signs, stupor, disorientation, coma, tremors, occasional convulsions (especially in infants) and spastic (but rarely flaccid) paralysis. Case-fatality rates range from 0.3% to 60%, with the rates due to Japanese (JE), Murray Valley (MV) and eastern equine encephalomyelitis (EEE) among the highest. Neurologic sequelae occur with variable frequency depending on age and infecting agent; they tend to be most severe in infants infected with JE, western equine encephalomyelitis (WEE) and EEE viruses. Mild leukocytosis is usual in these mosquito-borne diseases; leukocytes in the CSF, predominantly lymphocytes, range from 50 to 500/cu mm (SI units: 50 to 500 x 10^6/L) and may be 1,000/cu mm or greater (SI units: 1,000 x 10^6/L or greater) in infants infected with EEE virus. The elderly are at greatest risk of encephalitis with St. Louis encephalitis (SLE) or EEE virus infection, while children under 15 years of age are at greatest risk from LaCrosse virus infection and may develop seizures.

These diseases require differentiation from the tickborne encephalitides (see below); encephalitic and nonparalytic poliomyelitis; rabies; mumps meningoencephalitis; lymphocytic choriomeningitis; aseptic meningitis due to enteroviruses; herpes encephalitis; postvaccinal or postinfection encephalitides; and bacterial, mycoplasmal, protozoal, leptospiral and mycotic meningitides or encephalitides. Venezuelan equine encephalomyelitis, Rift Valley fever and West Nile viruses produce primarily arthropod-borne viral fever, but may sometimes cause encephalitis.

Identification is made by demonstrating specific IgM in acute-phase serum or CSF, or antibody rises between early and late specimens of serum by neutralization, CF, HI, FA, ELISA or other serologic tests. Cross reactions may occur within a virus group. Virus may occasionally be isolated by inoculation of suckling mice or cell culture with the brain tissue of fatal cases, rarely from blood or CSF after symptoms have appeared; histopathologic changes are not specific for individual viruses.

2. Infectious Agent

Each disease is caused by a specific virus in one of three groups: EEE and WEE in the alphaviruses (Togaviridae, Alphavirus); JE, Kunjin, MV encephalitis, SLE and Rocio encephalitis in the flaviviruses (Flaviviridae, Flavivirus); and LaCrosse, California

encephalitis, Jamestown Canyon and snowshoe hare viruses in the California group of bunyaviruses (Bunyaviridae, Bunyavirus).

3. Worldwide Occurrence

EEE is recognized in eastern and north central US and adjacent Canada, in scattered areas of Central and South America and in the Caribbean islands; WEE in western and central US, Canada and parts of South America; JE in western Pacific islands from Japan to the Philippines, rarely cases have occurred on Badu Island in the Torres Strait and in far North Queensland, Australia and in many areas of eastern Asia from Korea to Indonesia, China and India; Kunjin and MV encephalitis in parts of Australia and New Guinea; SLE in most of the US, in Ontario (Canada) and in Trinidad, Jamaica, Panama and Brazil; Rocio encephalitis in Brazil; LaCrosse encephalitis in the US from Minnesota and Texas east to New York and Georgia; snowshoe hare encephalitis in Canada, China and Russia. Cases due to these viruses occur in temperate latitudes in summer and early fall and are commonly limited to areas and years of high temperature and many mosquitoes.

4. Reservoir

California group viruses overwinter in *Aedes* eggs; the true reservoir or means of winter carryover for other viruses is unknown, possibly birds, rodents, bats, reptiles, amphibians or survival in mosquito eggs or adults, with the mechanisms probably differing for each virus.

5. Mode of Transmission

By the bite of infective mosquitoes. Most important vectors are:

- For EEE in the US and Canada, probably *Culiseta melanura* from bird to bird, and one or more *Aedes* and *Coquillettidia* spp. from birds or other animals to humans;
- For WEE in western US and Canada, *Culex tarsalis*;
- For JE, *C. tritaeniorhynchus*, *C. vishnui* complex and in the tropics, *C. gelidus*;
- For MV, probably *C. annulirostris*;
- For SLE in the US, *C. tarsalis*, the *C. pipiens-quinquefasciatus* complex and *C. nigripalpus*;
- For LaCrosse, *Ae. triseriatus*.

Mosquitoes, if not transovarianly infected, acquire virus, such as LaCrosse virus, from wild birds or small mammals, but pigs, as well as birds, are important for JE. LaCrosse virus is transovarianly and venereally transmitted in *Ae. triseriatus* mosquitoes.

6. Incubation period

Usually 5-15 days.

7. Period of communicability

Not directly transmitted from person to person. Virus is not usually demonstrable in the blood of humans after onset of disease. Mosquitoes remain infective for life. Viremia in birds usually lasts 2-5 days, but may be prolonged in bats, reptiles and amphibians, particularly if interrupted by hibernation. Horses develop active disease with the two equine viruses and with JE, but viremia is rarely present in high titer or for long periods; therefore, humans and horses are uncommon sources of mosquito infection.

8. Susceptibility and resistance

Susceptibility to clinical disease is usually highest in infancy and old age; inapparent or undiagnosed infection is more common at other ages. Susceptibility varies with virus, e.g., LaCrosse encephalitis is usually a disease of children, while severity of SLE increases with age. Infection results in homologous immunity. In highly endemic areas, adults are largely immune to local strains by reason of mild and inapparent infection; susceptibles are mainly children.

B. METHODS OF CONTROL

1. Preventive measures:

a. Educate the public as to the modes of spread and control.
b. Destroy larvae and eliminate breeding places of known and suspected vector mosquitoes, e.g., destroy or spray tires to prevent breeding of the LaCrosse vector.
c. Kill mosquitoes by space and residual spraying of human habitations (also see MALARIA, B1(I)a-c).
d. Screen sleeping and living quarters; use mosquito bed nets.
e. Avoid exposure to mosquitoes during hours of biting, or use repellents (see MALARIA, B1(II)1-4).
f. In endemic areas, immunize domestic animals or house them away from living quarters, e.g., pigs in JE endemic areas.
g. Mouse brain inactivated vaccine against JE encephalitis is used for children in Japan, Korea, Thailand, India and Taiwan. This vaccine is commercially available in the US and is recommended for those traveling to endemic areas for extended visits to rural areas. Live attenuated and formalin inactivated primary hamster kidney cell vaccines are licensed and widely used in China.
h. For those under continued intensive exposure in laboratory situations, EEE and WEE vaccines (inactivated, dried) are available from US Army Medical Research and Materiel Command, ATTN: MCMR-UMP, Fort Detrick, Frederick, MD 21702-5009 (telephone 301-619-2051).
i. Protect accidentally exposed laboratory workers passively with human or animal immune serum.

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority. Report under the appropriate disease; or as encephalitis, other forms; or as aseptic meningitis, with etiology or clinical type specified when known.
b. Isolation: None; virus is not usually found in blood, secretions or discharges during clinical disease. Enteric precautions are appropriate until enterovirus meningoencephalitis is ruled out.
c. Concurrent disinfection: None.
d. Quarantine: None.
e. Immunization of contacts: None.
f. Investigation of contacts and source of infection: Search for missed cases and the presence of vector mosquitoes; test for viremia in both febrile and asymptomatic family members. Primarily a community vector control problem (see B3, below).
g. Specific treatment: None.

3. Epidemic measures

a. Identification of infection among horses or birds and recognition of human cases in the community have epidemiologic value by indicating frequency of infection and areas involved. Immunization of horses probably does not limit spread of the virus in the community; immunization of pigs against JE should have a significant effect.
b. Fogging or spraying from aircraft with suitable insecticides has shown promise for aborting urban epidemics of SLE.

4. International measures

Spray with insecticide those airplanes arriving from recognized areas of prevalence. WHO Collaborating Centres.